

What is claimed is:

1. An composition comprising a first insulin species and a second insulin species, wherein the first insulin species and the second insulin species form a heterodimeric complex; and wherein the 5 first insulin species and the second insulin species are selected such that the heterodimeric complex is more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species.
2. The composition of claim 1, wherein the first insulin species is human insulin and the 10 second insulin species is a variant of human insulin having at least one amino acid substitution.
3. The composition of claim 2, wherein the variant of human insulin is LISPRO insulin.
4. The composition of claim 3, wherein the human insulin comprises from about 1% to about 15 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.
5. The composition of claim 4, wherein the human insulin comprises from about 5% to about 20 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.
6. The composition of claim 1, wherein the composition is a pharmaceutical composition.
7. The composition of claim 1, wherein the heterodimeric complex formed by the first insulin 25 species and the second insulin species is determined to be more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species by a spectrophotometric assay of turbidity.
8. The composition of claim 1, wherein the heterodimeric complex formed by the first insulin 30 species and the second insulin species is shown to be more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species by a Thioflavin-T assay.

9. A composition comprising a combination of a first insulin species and a second insulin species, wherein the first and second insulin species are selected to generate a composition that is more stable than a composition having only the first insulin species or a composition having only
5 the second insulin species.

10. The composition of claim 1, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.

10 11. The composition of claim 10, wherein the variant of human insulin is LISPRO insulin.

12. The composition of claim 11, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.
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13. The composition of claim 12, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.
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14. The composition of claim 9, wherein the composition is a pharmaceutical composition.

15. A method of making an insulin composition, comprising combining a first insulin species and a second insulin species, wherein the first insulin species and the second insulin species form a heterodimeric complex; and wherein the first insulin species and the second insulin species are
25 selected such that the heterodimeric complex is more stable than a homodimeric complex formed by the first insulin species or a homodimeric complex formed by the second insulin species.

16. The method of claim 15, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.
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17. The method of claim 16, wherein the variant of human insulin is LISPRO insulin.

18. The method of claim 17, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

5 19. The method of claim 12, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

20. The method of claim 15, wherein the composition is a pharmaceutical composition.

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21. A method of stabilizing an insulin composition, comprising combining a first insulin species and a second insulin species, wherein the first and second insulin species are selected to generate a composition that is more stable than a composition having only the first insulin species or a composition having only the second insulin species.

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22. The method of claim 21, wherein the first insulin species is human insulin and the second insulin species is a variant of human insulin having at least one amino acid substitution.

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23. The method of claim 22, wherein the variant of human insulin is LISPRO insulin.

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24. The method of claim 23, wherein the human insulin comprises from about 1% to about 50% of the insulin of the composition and wherein the LISPRO insulin comprises from about 50% to about 99% of the insulin of the composition.

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25. The method of claim 24, wherein the human insulin comprises from about 5% to about 20% of the insulin of the composition and wherein the LISPRO insulin comprises from about 95% to about 80% of the insulin of the composition.

26. The method of claim 25, wherein the composition is a pharmaceutical composition.

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27. A method for identifying a stabilized insulin composition comprising the steps of combining a first insulin species with a second insulin species so that a heterodimeric complex formed from the

first and second insulin species is generated, comparing the stability of the heterodimeric complex formed from the first and second insulin species with the stability of a homodimeric complex formed from the first insulin species or a homodimeric complex formed from the second insulin species and identifying a formulation wherein the heterodimeric complex formed from the first and 5 second insulin species is more stable than homodimeric complex formed from the first insulin species or a homodimeric complex formed from the second insulin species.

28. The method of claim 27, wherein the heterodimeric complex formed by the first insulin species and the second insulin species is shown to be more stable than a homodimeric complex 10 formed by the first insulin species or a homodimeric complex formed by the second insulin species in a spectrophotometric assay of turbidity.

29. The method of claim 27, wherein the heterodimeric complex formed by the first insulin species and the second insulin species is shown to be more stable than a homodimeric complex 15 formed by the first insulin species or a homodimeric complex formed by the second insulin species in an assay with Thioflavin-T.

30. A method for identifying a stabilized insulin composition comprising the steps of combining 20 a first insulin species with a second insulin species and comparing the stability of the formulation having a combination of the first and second insulin species with the stability of a formulation having only the first insulin species or a formulation having only the second insulin species and identifying an insulin composition wherein the formulation generated by combining the first and second insulin species is more stable than a formulation having only the first insulin species or a formulation having only the second insulin species.

31. The method of claim 30, wherein the formulation having a combination of the first and second insulin species is determined to be more stable than a formulation having only the first insulin species or a formulation having only the second insulin species by a spectrophotometric assay of turbidity.

32. The method of claim 30, wherein the formulation having a combination of the first and second insulin species is determined to be more stable than a formulation having only the first insulin species or a formulation having only the second insulin species by a Thioflavin-T assay.